

10/509036

Figure 1

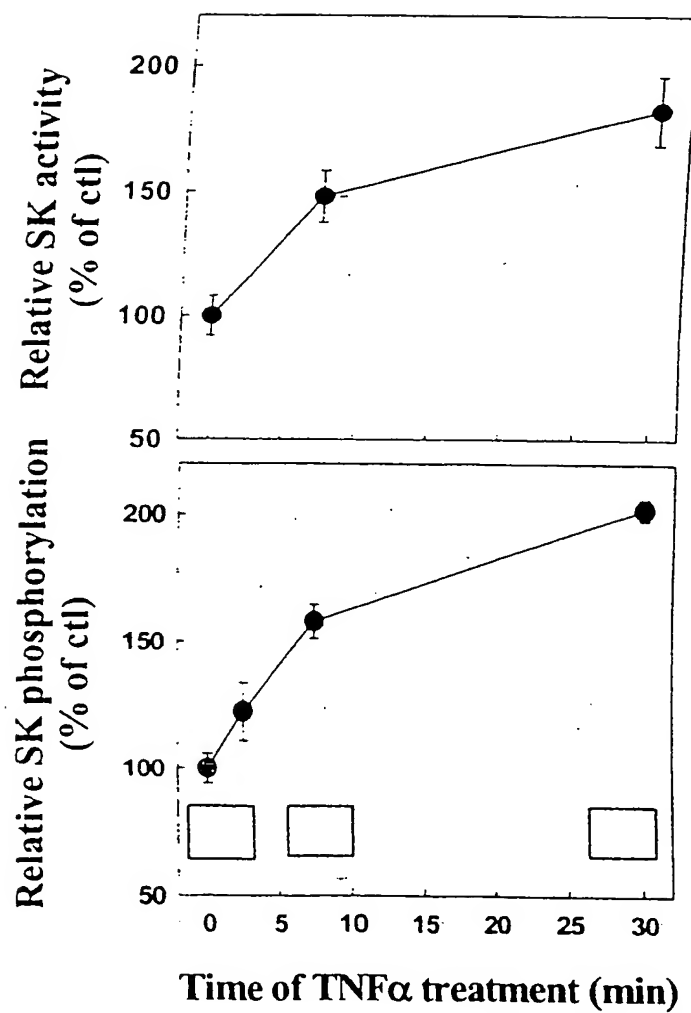


Figure 2

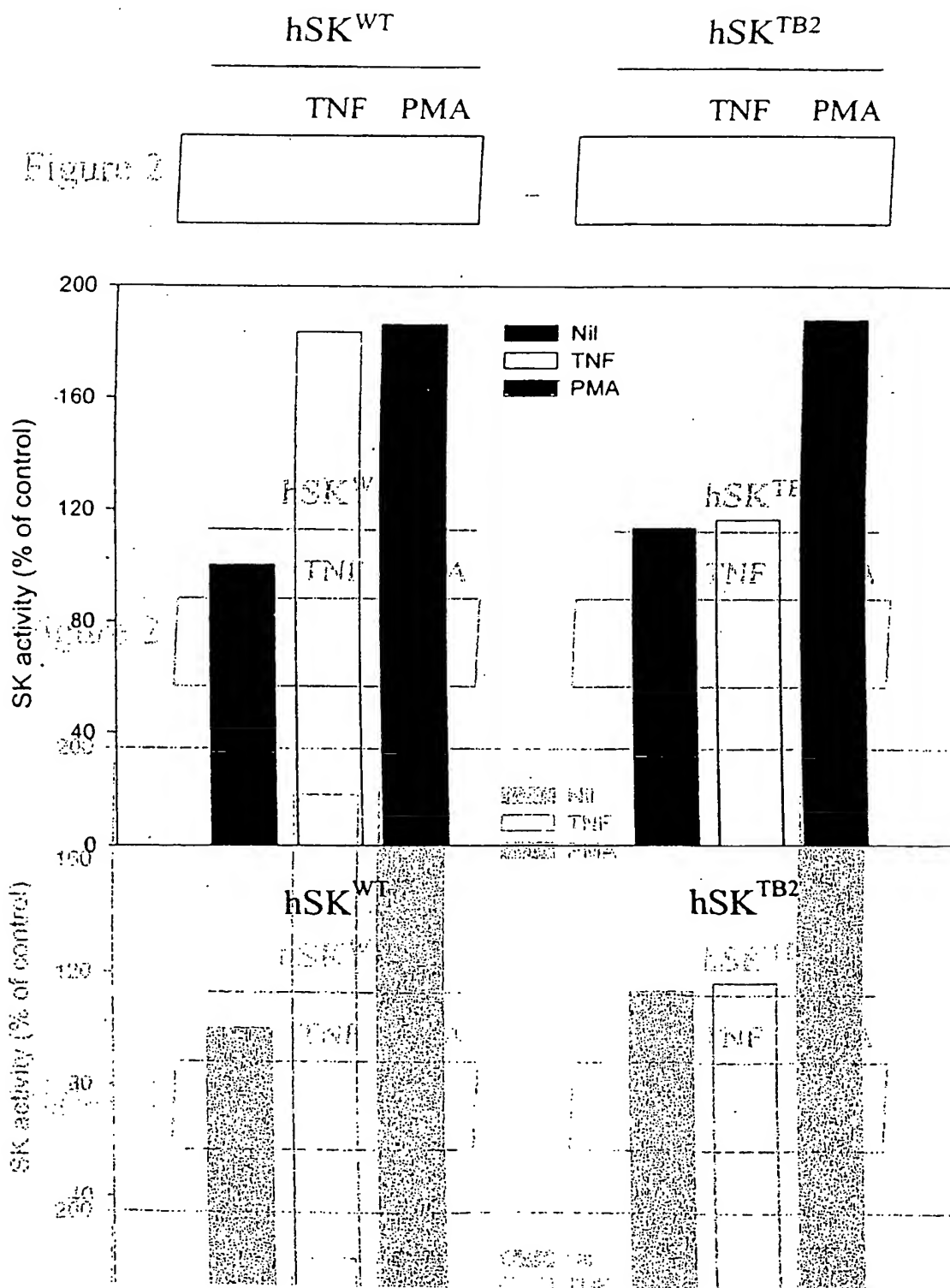


Figure 3

1 MDPAGGPRGVLPPCRVLVLLNPRGGKGKALQLFRSHVQPLLAAEAEISFTLMLTERRNHARELVSRSEELG 70  
71 RWDALVVMGSGDGLMHEVVNGLMERPDWETAIQKPLCSLPAGSGNALAASLNHYAGYEQVTNEDLLTNCTL 140  
141 LLCRRLLSPMNL LSLHTASGLR LFSVLSLAWGFIADV DLESEFKYPRRLGEMRFTLTGTLRLAALRTYRGRL 210  
211 AYL PVGRVGSKTPASPVVVQQGPVDAHLVPLEEPVPSHNTVVPDEDFVLVLLHSHLGSEMFAAPMGRC 280  
281 AAGVMHLFYVRAGVSRAMLLRLFLAMEKGRHMEYECPYLVVVPVVAFRLEPKDGKGMFAVDGELMVSEAV 350  
351 QGVHPNYPWMVSGCPEPPPSWKPPQMPPEEPL 384

Figure 4

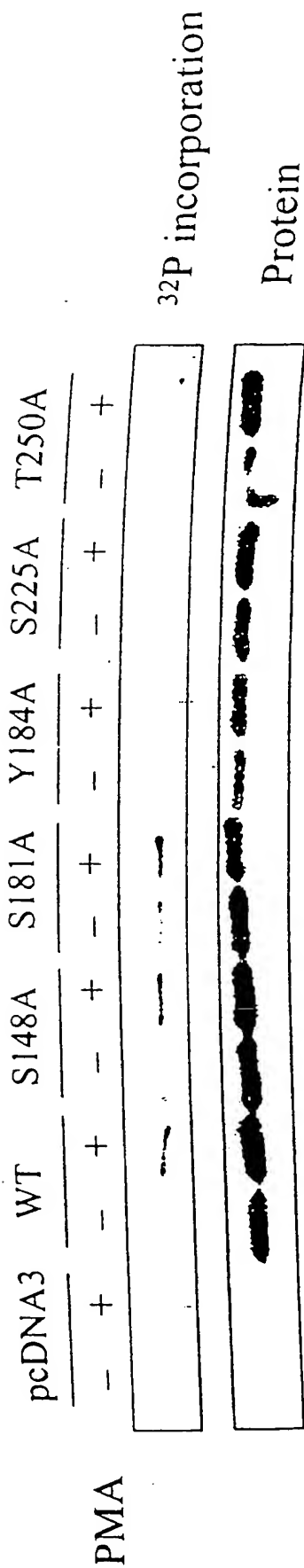


Figure 5

	<u>hSK<sup>S225A</sup></u>		<u>hSK<sup>WT</sup></u>		<u>hSK<sup>S220A</sup></u>		<u>hSK<sup>T222A</sup></u>	
PMA	-	+	-	+	-	+	-	+

Figure 6

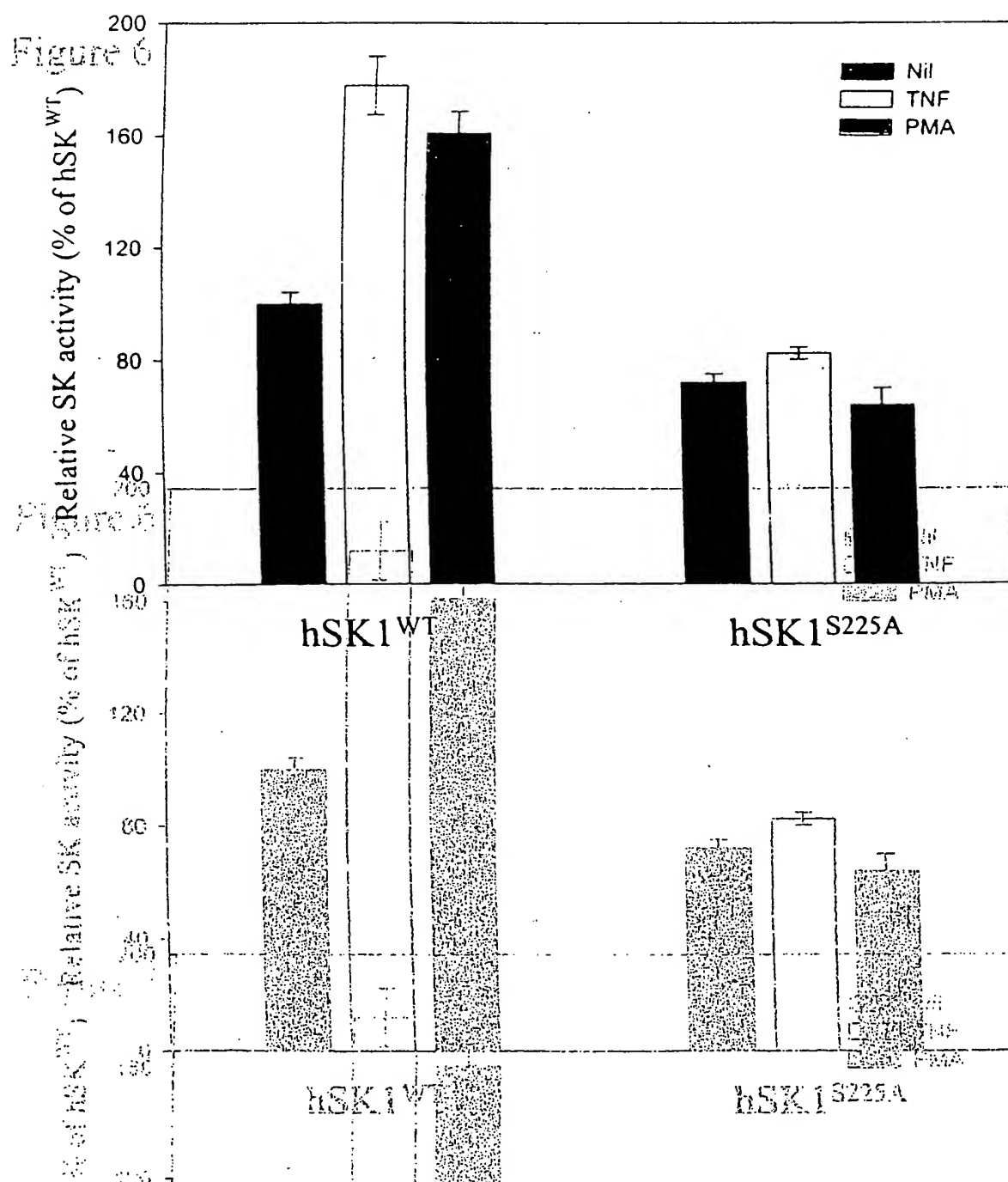


Figure 7

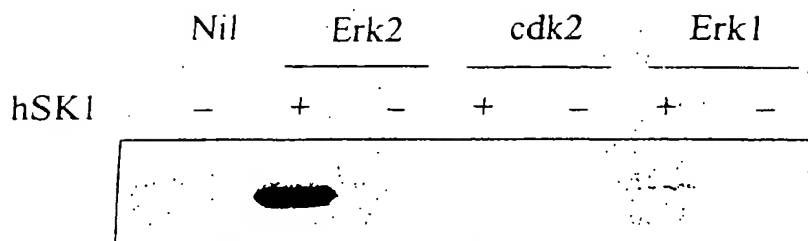


Figure 7

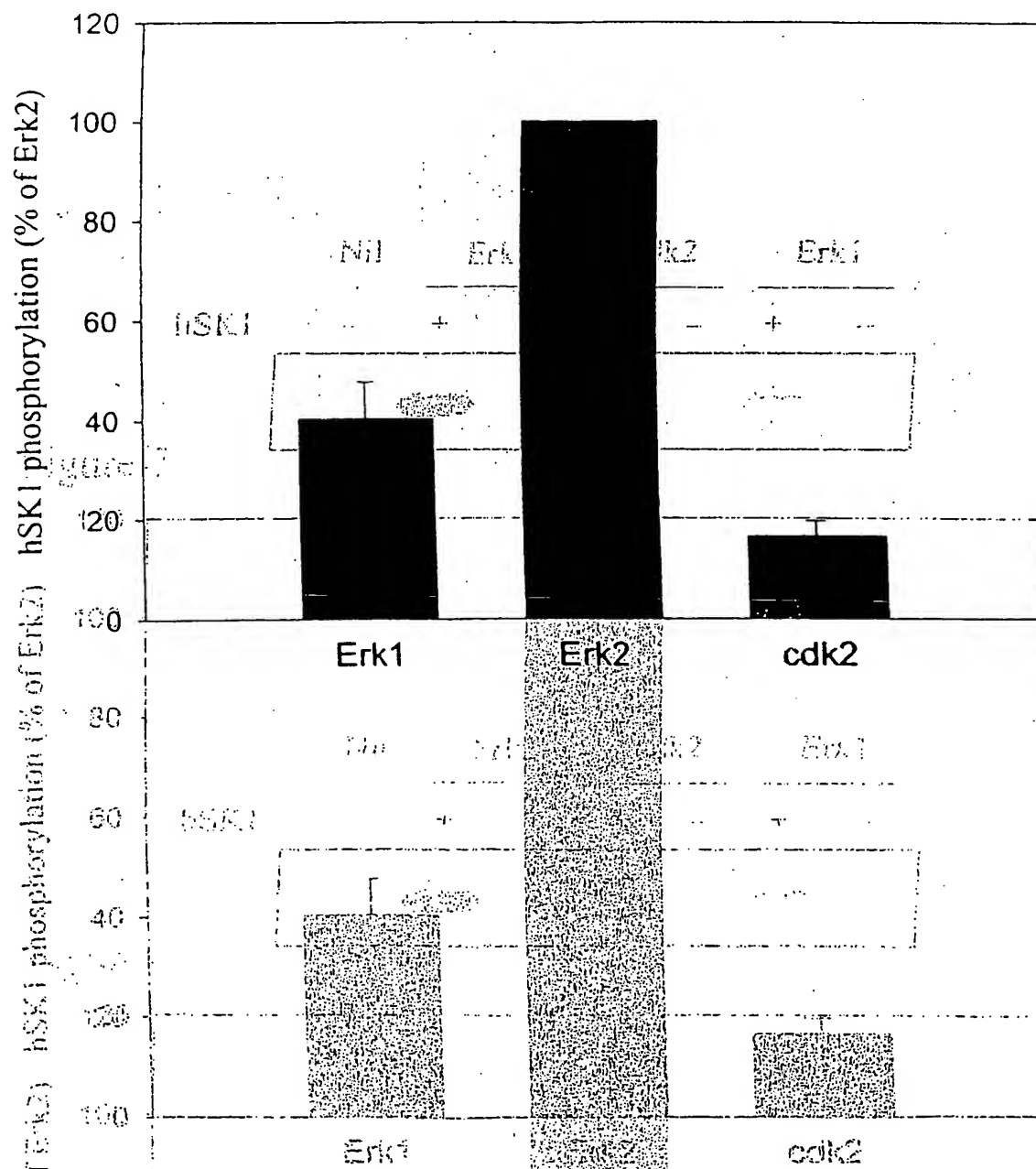


Figure 8

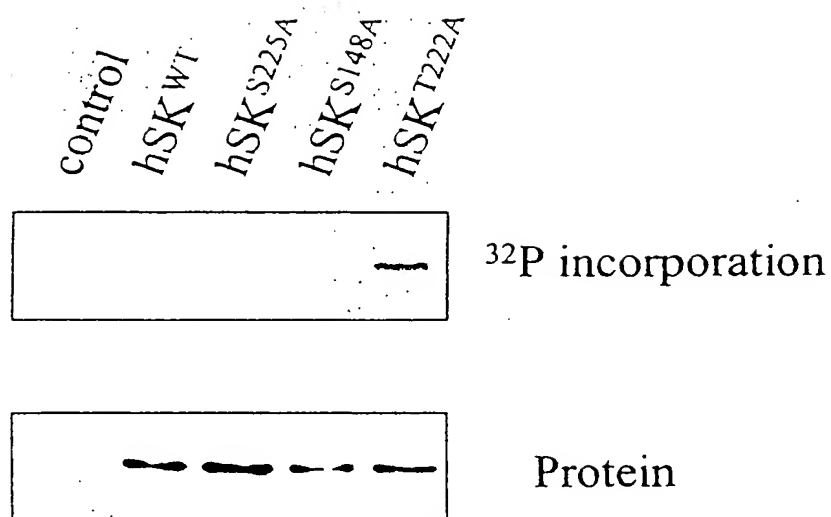




Figure 9

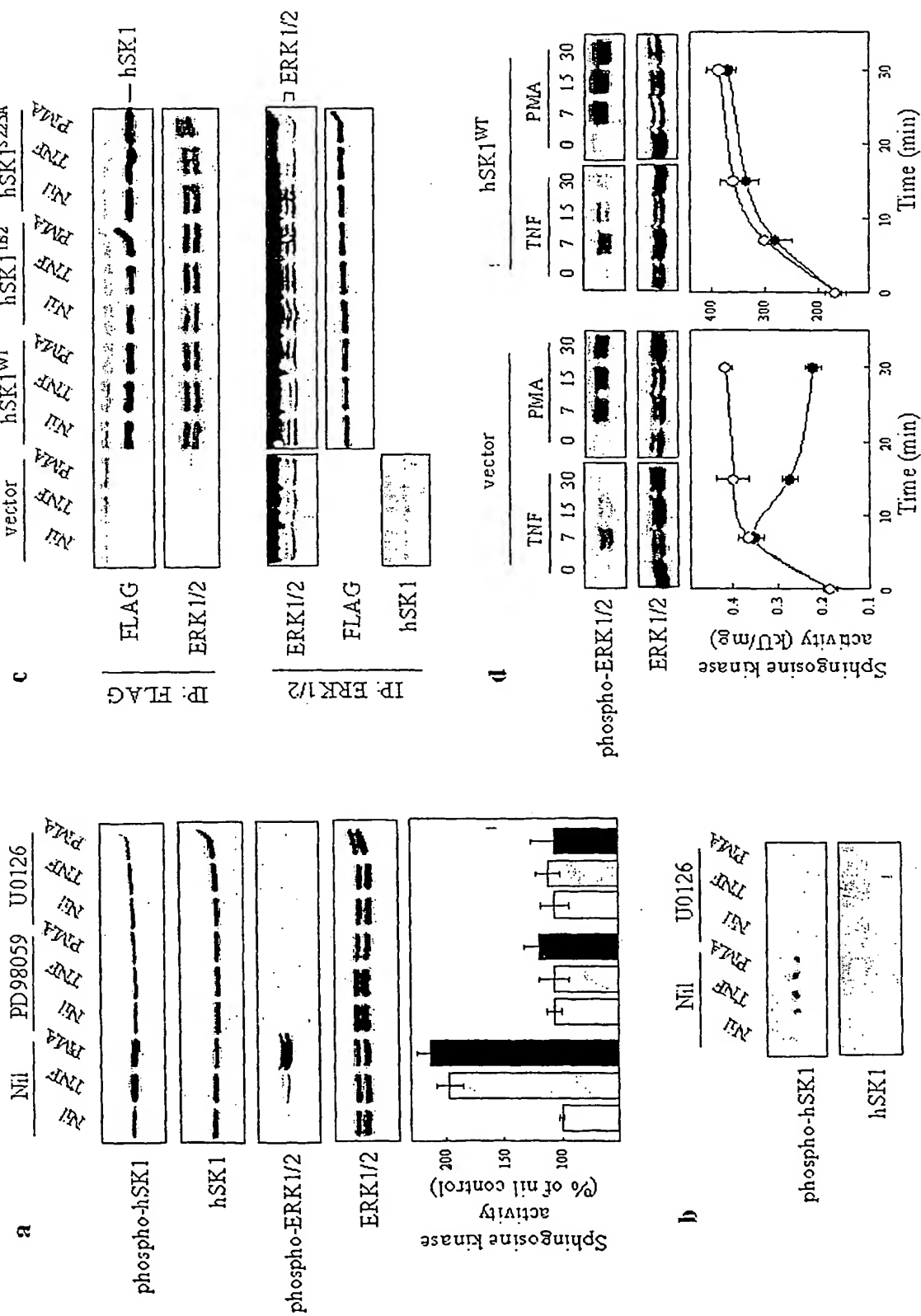


Figure 10A

Figure 10A

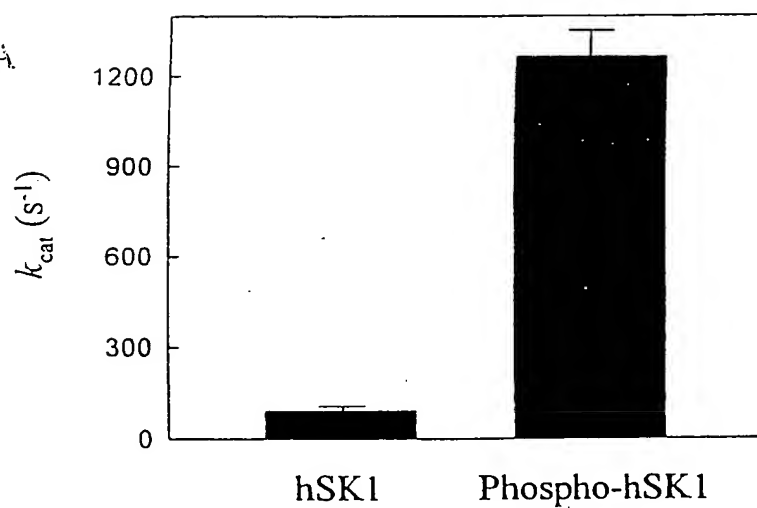


Figure 10A

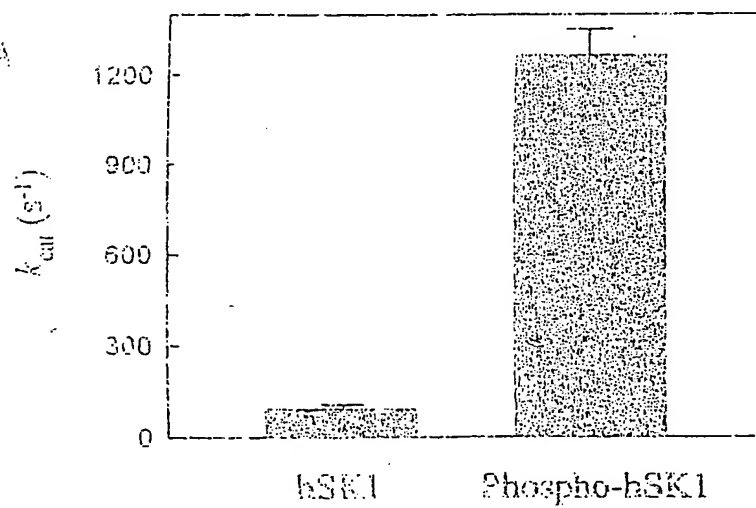


Figure 10A

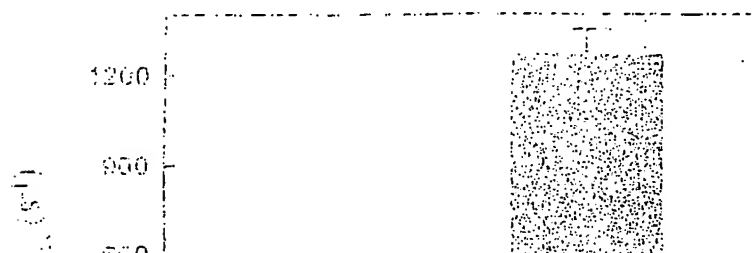


Figure 10B

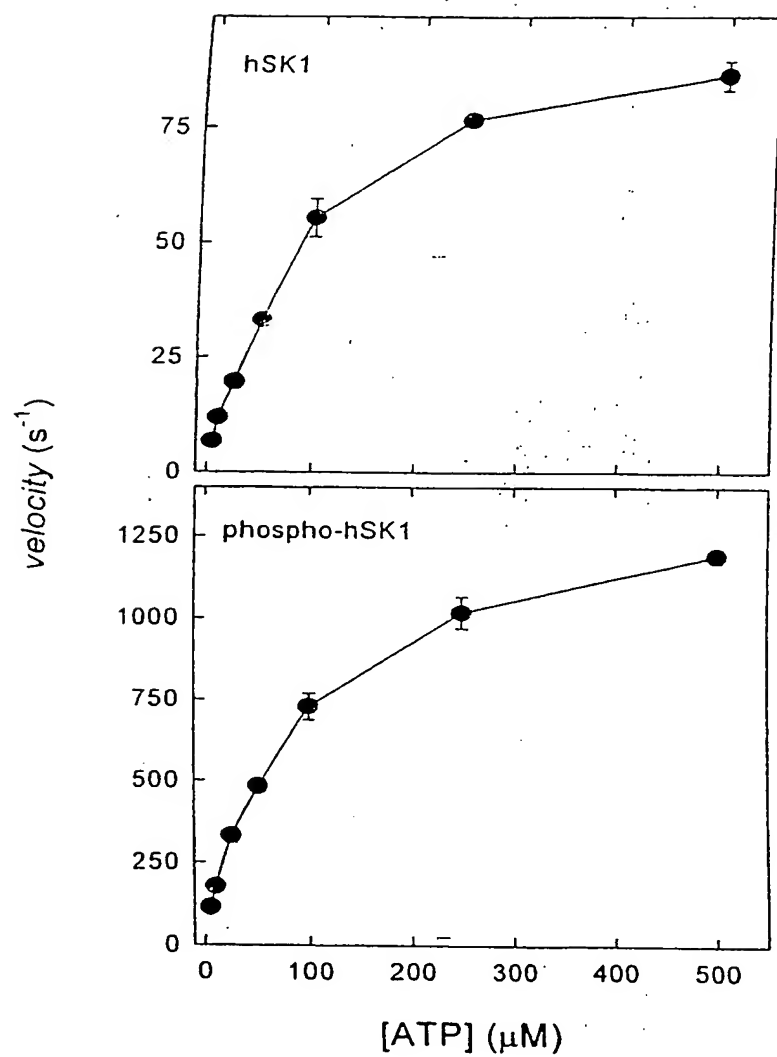


Figure 10C

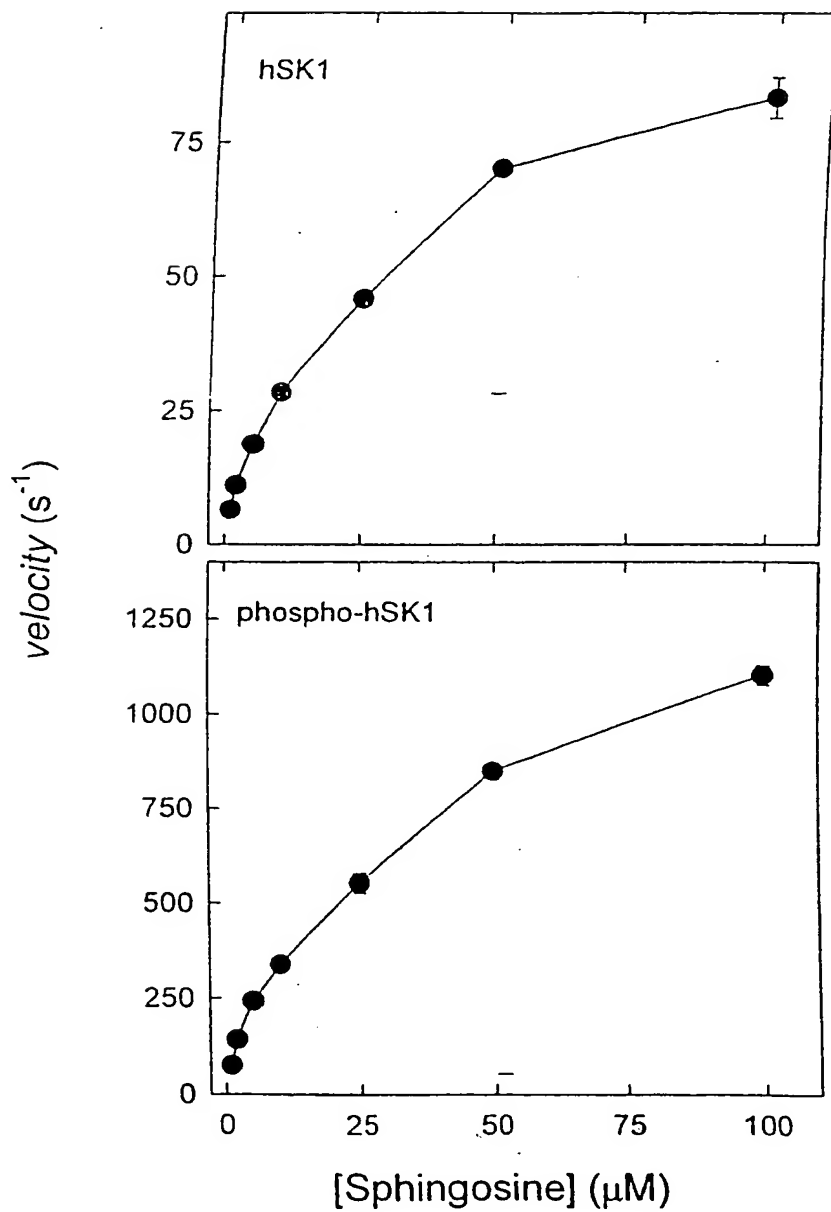


Figure 11

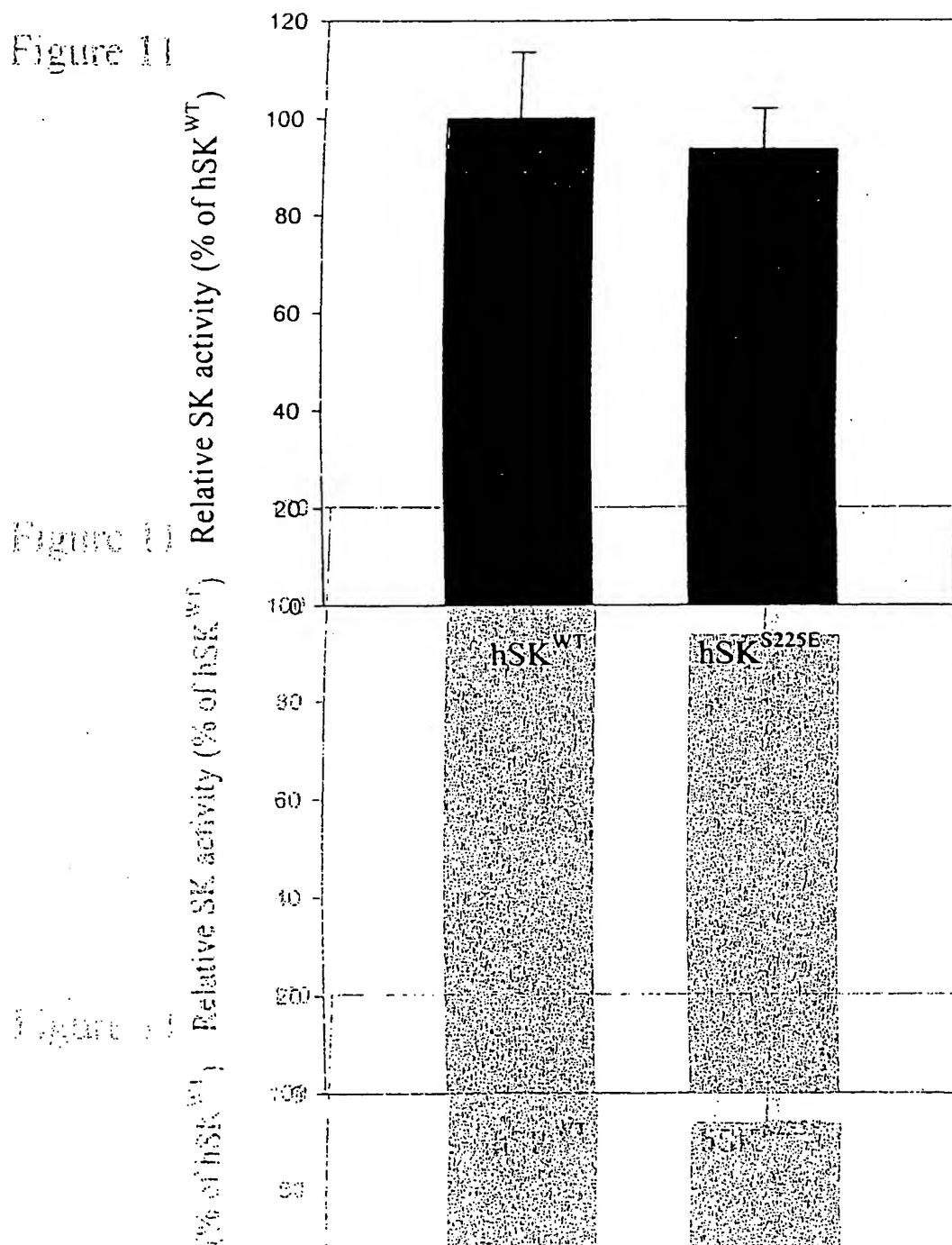


Figure 12

antagonists directly targeting the catalytic activity

(eg. Drugs targeting ATP or Sphingosine binding sites)

ATP Sphingosine

antagonists targeting activation

hSK1

Protein kinase  
(Erk2?)

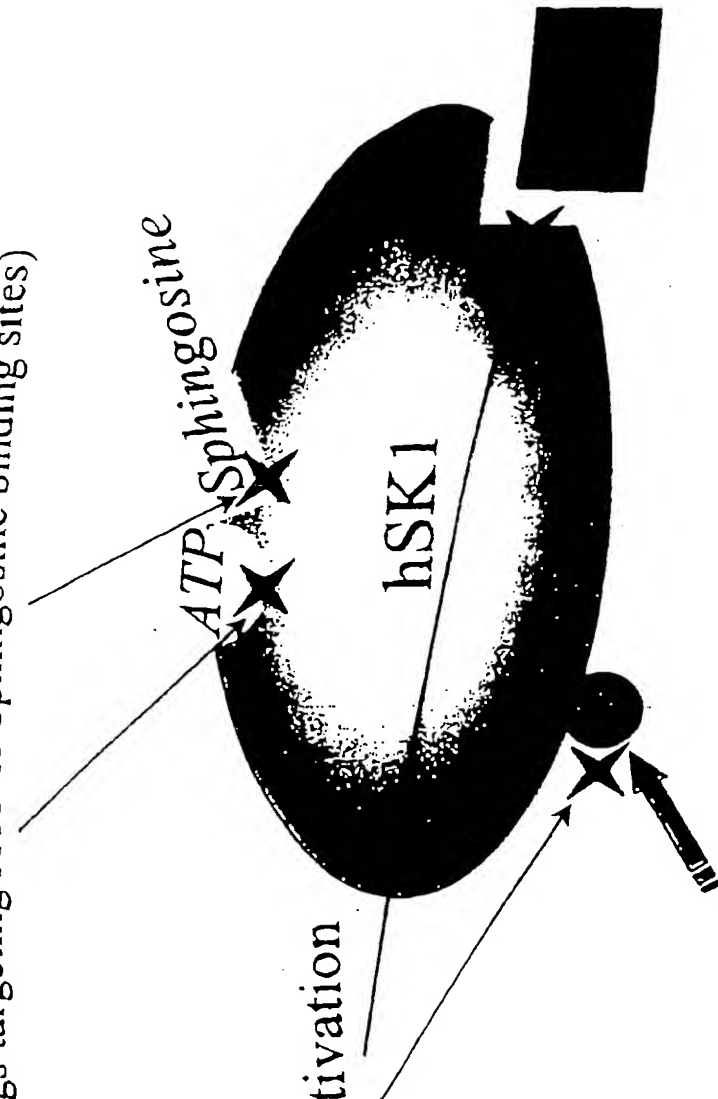


Figure 13

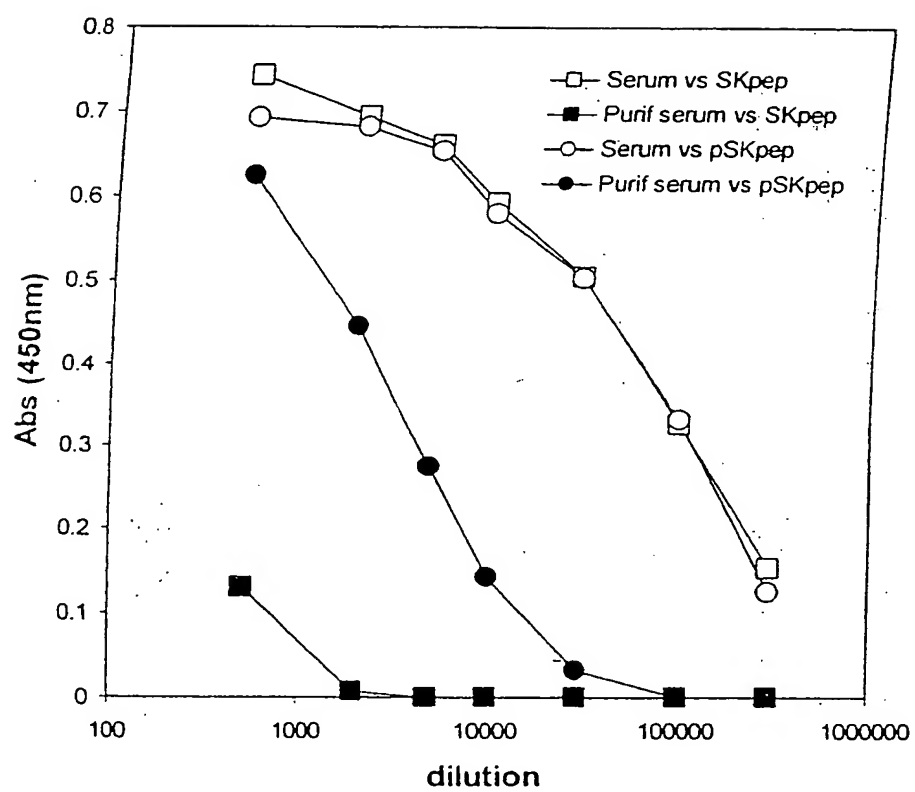


Figure 14

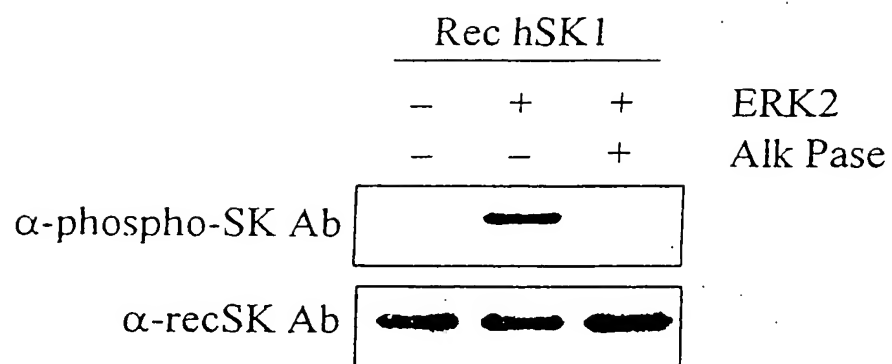




Figure 15

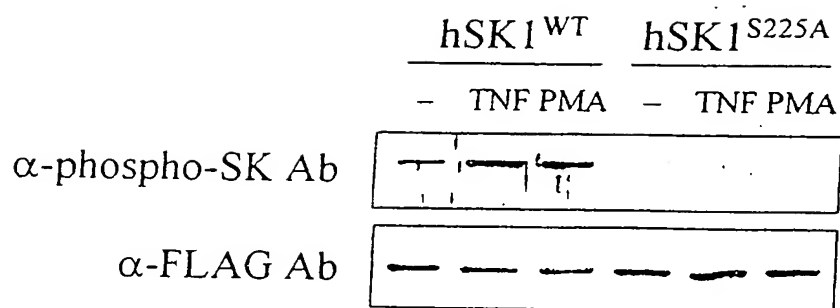


Figure 16

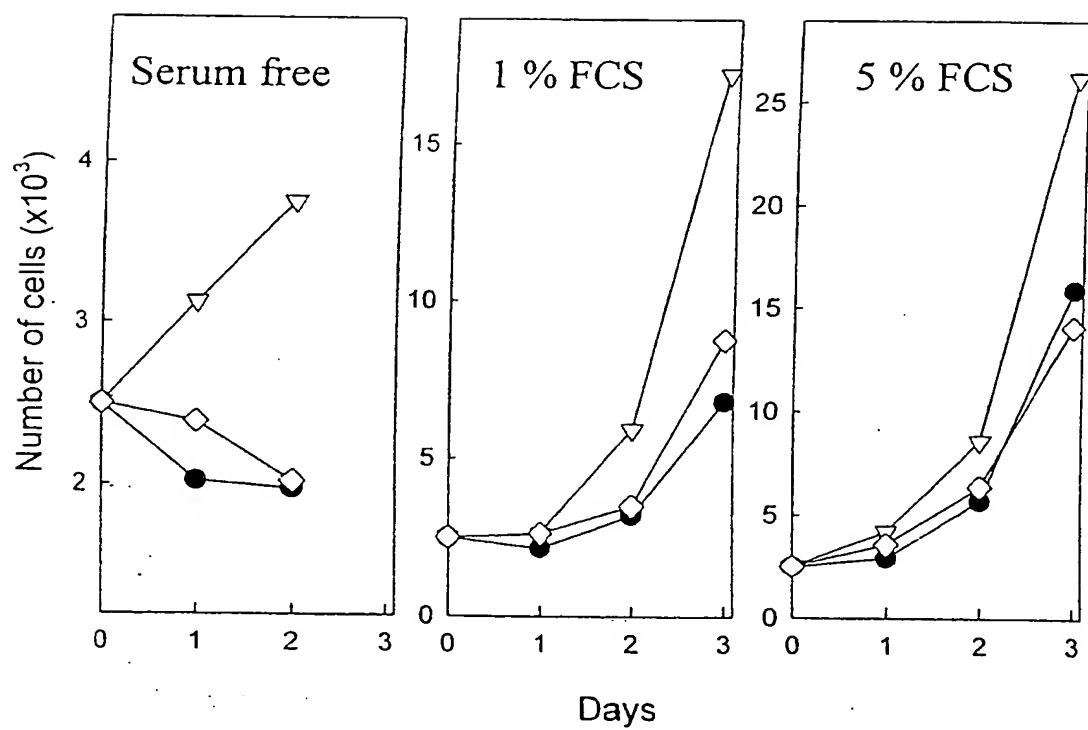
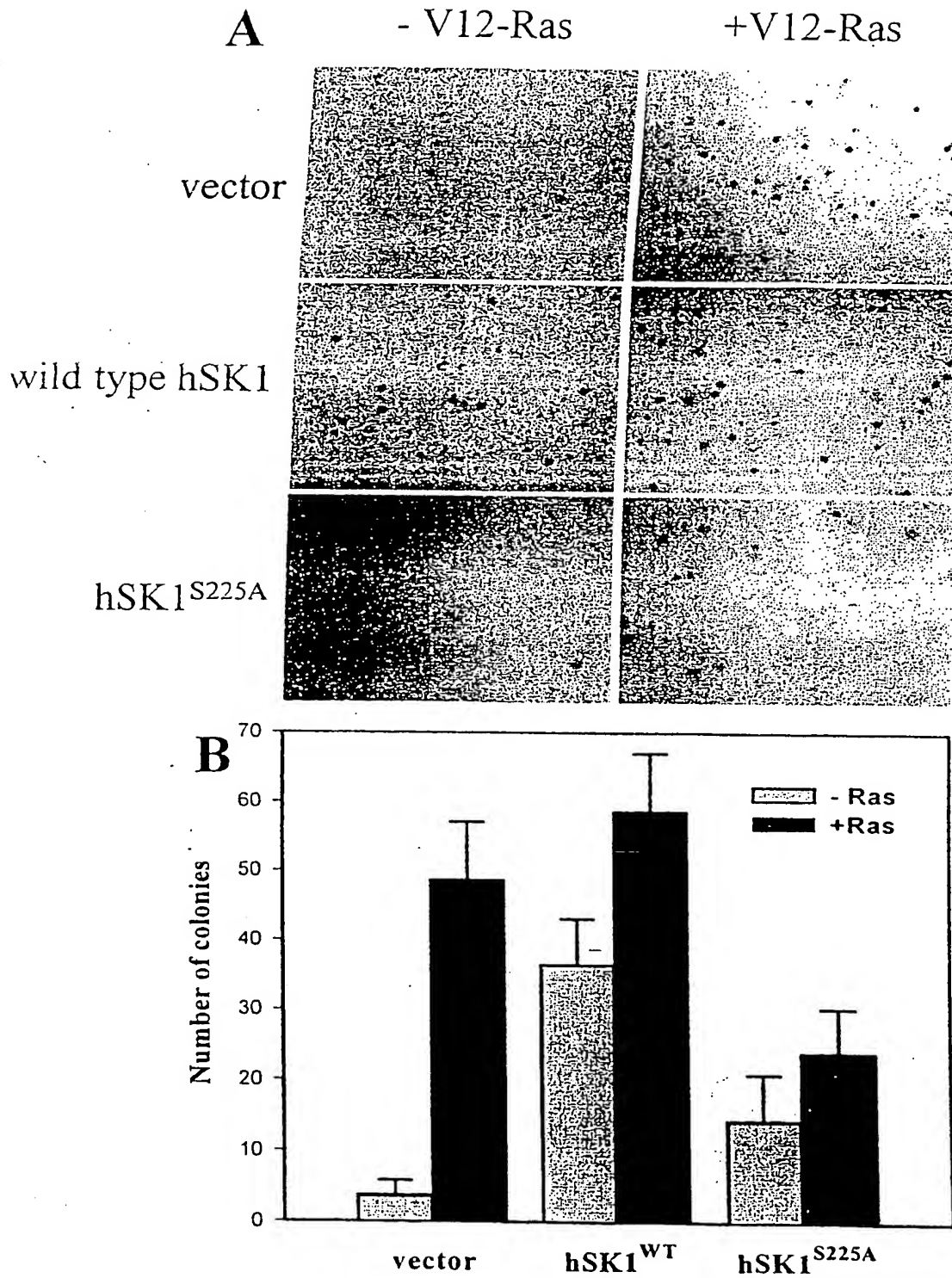


Figure 17



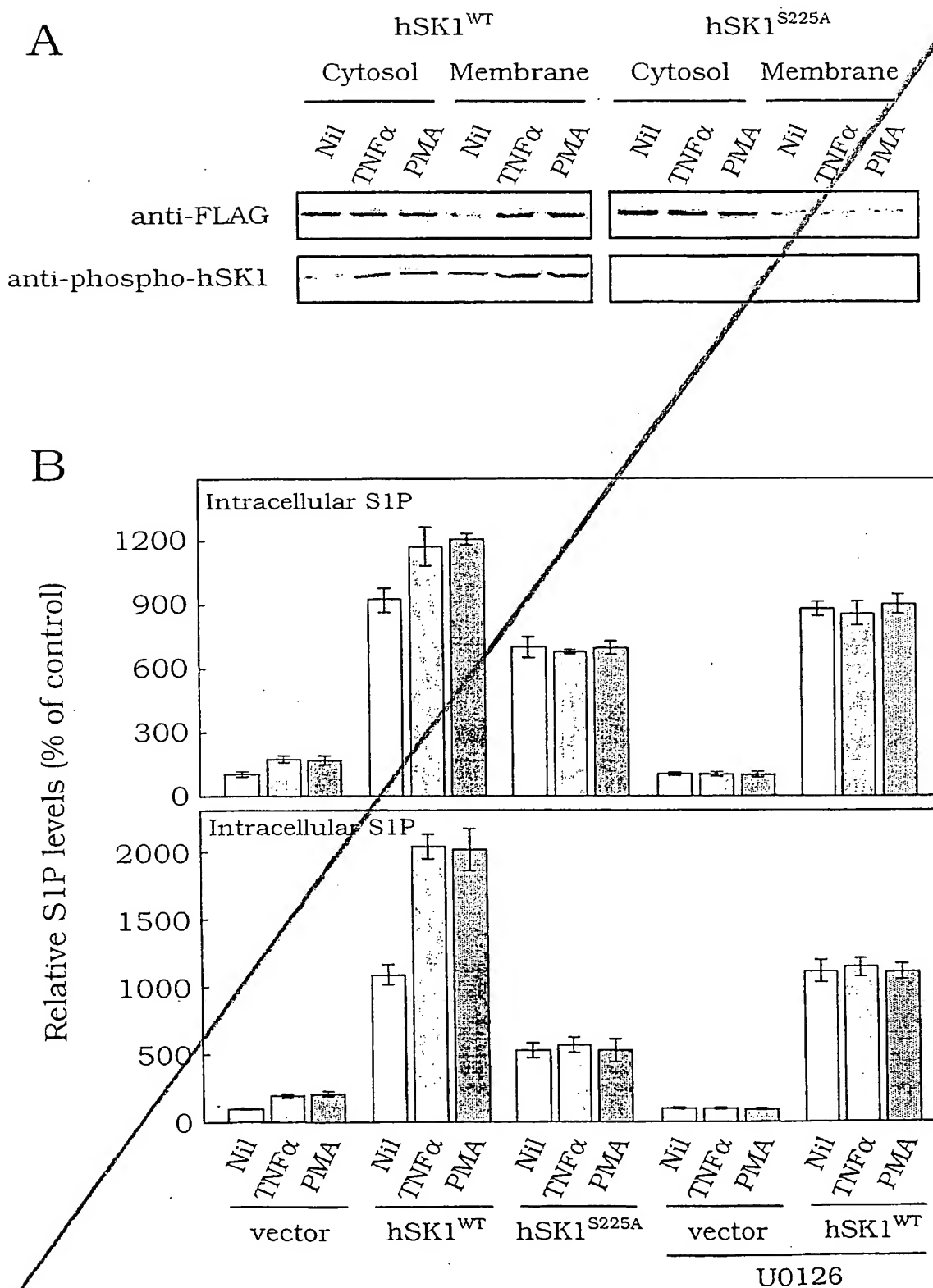


Figure 18

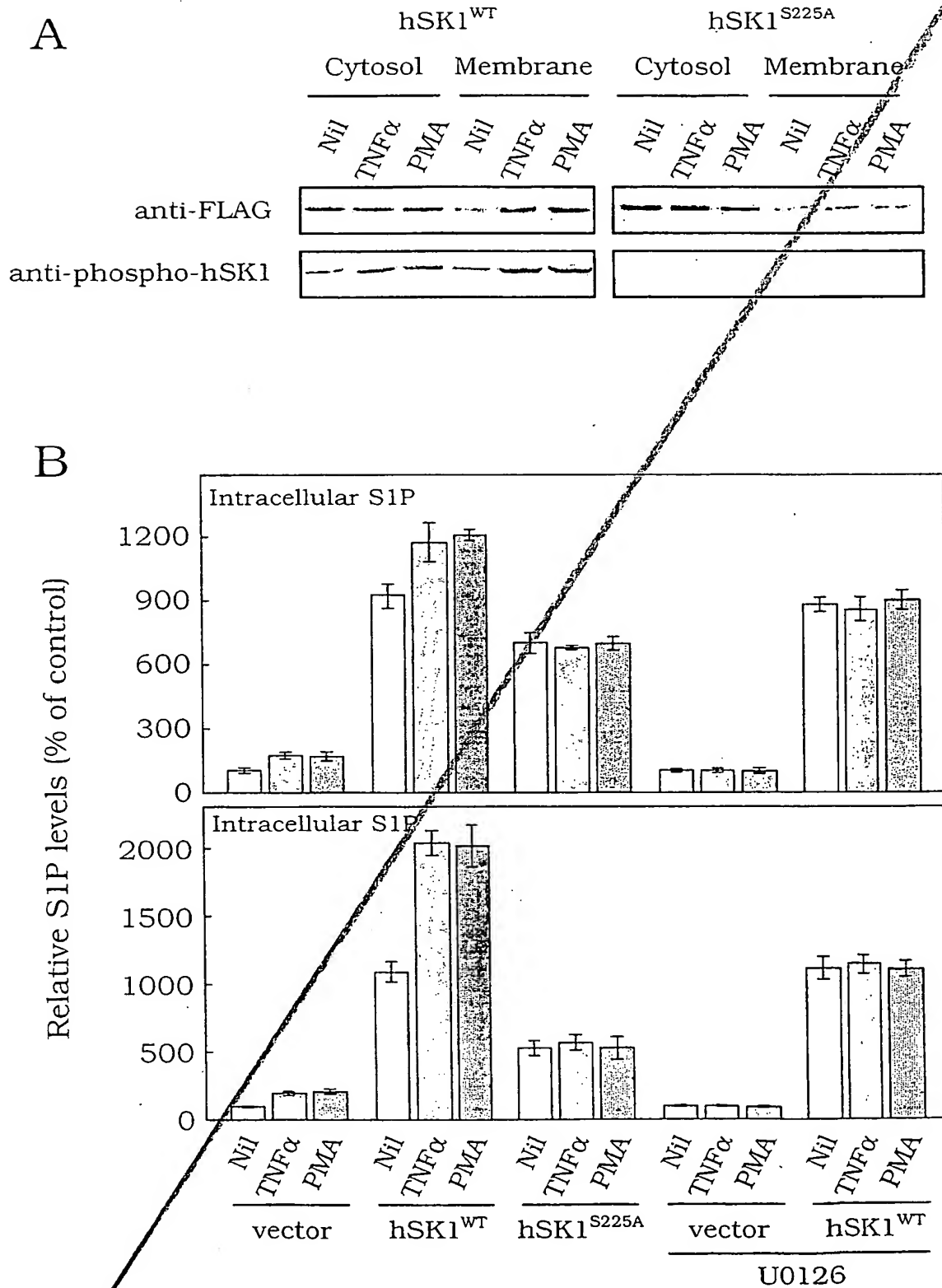


Figure 18